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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,051	02/14/2001	Derek N.J. Hart	659-37	1833

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 05/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/782,051	HART, DEREK N.J.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 13-18* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☐ Claim(s) *4-8 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 11/12/03 has been acknowledged.

Claims 9-12 are canceled.

Claims 4-8 and 18 are amended.

Claims 1-8, 13-18 are pending

This application contains claims 1-3 and 13-17 are drawn to an invention nonelected with traverse in Paper No. 02/05/03. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 4-8 and 18 are examined in this office action.

Applicants are required to follow Amendment Practice under revised **37 CFR §1.121**. The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.

Claim Rejections - 35 USC § 101

1. Claims 4-8 and 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well-established utility for the same reasons of record as set forth in the office action mailed on 05/08/03.

The instant claims are drawn to an isolated DNA sequence, which encodes an enzyme according to SEQ ID NO:1 or a functional portion equivalent thereof. The claims are further drawn to a DNA sequence comprises nucleotides 529-945, 549-1844 or 1-1844 of SEQ ID NO:1.

Response to arguments

The applicant argues that the isolation of novel variance of AHCY, such as DD4b5.3, is inherently useful. The identification of novel variants of AHCY provides for the dissection of the mechanisms that underlie normal and abnormal biological functions associated with this enzyme. This, combined with the discovery that expression of DD4b5.3 is restricted largely to dendritic-cells, would cause a skilled in

the art to understand that novel AHCY variants would be very useful, for example for the design of new drugs with immunomodulatory activity (response page 5-6).

However, applicant's argument are found NOT persuasive because the applicant fails to provide any evidence that the nucleic acid sequence of SEQ ID NO:1 encodes a polypeptide that has AHCY-like activity explicitly or implicitly as putatively considered by the applicant. The asserted AHCY-like nucleic acid sequences is mere a computer-generated hypotheses, since no biological function has been established for the nucleotides of SEQ ID NO:1. The specification fails to disclose any functional assay that would enable one skill in the art how to evaluate the biological activity of the AHCY-like enzyme encoded by the claimed nucleotide sequences. In addition the specification fails to establish any nexus between a disease and the claimed AHCY-like activity.
The office has provided clear evidence that the disclosed amino acid sequences matches with a AHCY-like protein (Human SAHH, AC:W90061, US5854023), but with amino acid sequence similarity of only 80.7%. In addition the state of art at the time of filing teaches that even though DD4b5.3 (SEQ ID NO:1) encodes an ACHY-like molecule the gene structure differs from that of AHCY (Dekker et al, Immunogenetics 53;993-1001, 2002., see page 998, col.2 para.2). Furthermore, the differences between AHCY and DCAL (encoded by SEQ ID NO:1 as claimed) protein and gene structure strongly suggest that DCAL has a different substrate (see page 1000, col.2 , para 4).
Considering the state of art and lack of specific guidance in the instant specification it is unclear how one skill in the art would use the invention as claimed, since the specification fails to disclose a single functional assay for the enzyme activity encoded by the nucleotide sequences of SEQ ID NO:1.

The instant specification does not comply with 35 U.S.C. 101 and 112 since nebulous expressions "biological activity" and "biological properties" do not contain a sufficiently explicit indication of usefulness of compounds and how to use them. The utility requirements must be met at the time of filing and not after someone else identify a utility that had not been disclosed in the specification. The disclosure is insufficient where experimentation is necessary to determine actual uses, or possible lack of uses, of compounds, as well as how to employ them in a useful manner. For example, it

cannot be presumed that a steroid chemical compound is "useful" under 35 U.S.C. 101, or that one skilled in the art will know "how to use" it, simply because compound is closely related only in a structural sense to other steroid compounds known to be useful (In re Kirk and Petrow, 153 USPQ 48 (CCPA 1967)). In instant case the mere presence of AHCY-like domain does not teach one skill in the art how to use the claimed invention, since the disclosure is insufficient and requires further experimentation necessary to determine actual uses or possible lack of uses of the encoded polypeptide, as well as how to employ them in a useful manner. It cannot be presumed that a AHCY-like domain bearing polypeptide is useful under 35 USC 101/112 or that one skilled in the art will know "how to use" it, simply because polypeptide is closely related only in a structural sense to other AHCY-like proteins known to be useful.

In view of the foregoing, one skilled in the art would not readily attribute any particular AHCY-like activity encoded by the instant nucleic acid in view of the low sequence similarity and the lack of sequence conservation therein. Therefore, the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function can be ascribed to the gene product. The only immediate apparent utility for the instant invention would be further scientific characterization of the claimed amino acid sequences a putative AHCY-like activity.

Claim Rejections - 35 USC § 112

2. Claims 4-8 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons of record as set forth in the office action mailed on 05/08/03.

Nature Of Invention:
Invention relates to a DNA sequence encoding an AHCY-like enzyme activity.

Breadth Of Claims And Guidance Provided By The Inventor:

The instant claims are drawn to an isolated DNA sequence, which encodes an enzyme having AHCY-type activity or a functional portion or a equivalent thereof. Claims are drawn to a DNA sequence that comprises nucleotides 529-945, 549-1844 or 1-1844 of SEQ ID NO:1. Claims are further drawn to a DNA construct comprising DNA sequence encoding an enzyme having AHCY-type activity. Claims are further drawn to a DNA construct that comprises an open reading frame coding for at least a functional portion of enzyme encoded by SEQ ID NO:1. Claims are further drawn to a DNA construct that comprises non-coding region of a gene coding according to SEQ ID NO:1. In addition the claims are drawn to a nucleic acid probe capable of hybridizing under high stringency conditions to the nucleotide sequences of SEQ ID NO:1.

The specification asserts that the nucleic acid as claimed encodes a polypeptide that has AHCY-type activity. The specification teaches that nucleotide sequence of SEQ ID NO:1 or DD4b5.3 (573-1845) has 52% amino acid similarity to human AHCY sequences and shares many conserved features critical for AHCY function (spec. page 3, lines 21-27, fig-2 and 3). The specification further teaches that the expression of such AHCY-like polypeptide in various cell lines and normal cell populations (spec. page 12-13, table 1 and 2). Based upon amino acid sequence similarities the instant specification concluded that the invention as claimed relates to an AHCY-type enzyme activity.

However, the instant specification fails to establish that that the disclosed polynucleotide sequences encodes an amino acid sequences which has AHCY-like activity explicitly or implicitly as putatively considered by the instant specification. The asserted enzyme AHCY-like activity is mere a computer-generated hypotheses, since no biological function has been established for the nucleotides of SEQ ID NO:1. The specification fails to disclose any functional assay that would enable one skill in the art how to evaluate the biological activity of the AHCY-like enzyme encoded by the claimed nucleotide sequences. In addition the specification fails to establish any nexus between a disease and the claimed AHCY-like activity. It is unclear whether the disease in question would be the result of the loss of AHCY-activity or is the result of altered protein function. It is even unclear whether the treatment of the disease associated with the polypeptide as claimed would require increase or decrease in the expression of the AHCY-like activity. Even though the specification teaches the nucleotide sequence of SEQ ID NO:1, the specification fails to define the open reading frame with a stop codon and the identification of an initiation of codon in SEQ ID NO:1. The specification even fails to disclose a single nucleotide sequence, which represent a complement, reverse complement and/or a reverse sequence base upon AHCY-like enzyme activity of the nucleotide sequence as claimed. The specification fails to teach any and all open reading frames in a sense or an anti-sense orientation encoding a gene that have AHCY-like enzyme activity. In addition the specification fails to define any non-coding region in the nucleotide sequences of SEQ ID NO:1. Furthermore the instant specification fails to teach any use of the claimed "reverse complement and reverse sequences", since these sequences would not hybridize to SEQ ID NO:1 or its complement. In addition, the specification fails to define the high stringency conditions

for any and all nucleotide sequence(s) that hybridize to polynucleotide encoding SEQ ID NO: 1. The specification fails to define the salt concentration in the hybridization and washing buffers In addition, the specification fails to disclose a set of temperature conditions specifically required for high stringency hybridization and washing steps. It is not clear how one skilled would use any set of hybridization conditions to form a detectable hybridization complex. On the other hand, the specification fails to disclose that any and all set of hybridization conditions would result in the detection of polynucleotide encoding SEQ ID NO:1 using the labeled nucleic acid probe as claimed. Therefore considering the applicant's disclosure it is unclear how one skill in the art would use the invention as claimed.

State Of Art And Predictability:

The office sequence search using the disclosed amino acid sequences provided matches with a AHCY-type activity-like protein (Human SAHH), but with only 83% similarity with amino acid sequences encoded by SEQ ID NO:1. Further inspection of the comparison shows limited if any areas of conservation between the two sequences. The state of art at the time of filing teaches that even though DD4b5.3 (SEQ ID NO:1) encodes an ACHY-like molecule the gene structure differs from that of AHCY (Dekker et al, Immunogenetics 53;993-1001, 2002., see page 998, col.2 para.2). Furthermore, the differences between AHCY and DCAL (encoded by SEQ ID NO:1) protein and gene structure strongly suggest that DCAL has a different substrate (page 1000, col.2 , para 4). Considering the state of art and lack of specific guidance in the instant specification it is unclear how one skill in the art would use the invention as claimed, since the specification fails to disclose a single functional assay for the enzyme activity encoded by the nucleotide sequences of SEQ ID NO:1. In addition, the scope of invention as claimed encompasses any and all functional variants of nucleotide sequences encoding AHCY-like activity. The variations as claimed encompasses the conserved motifs that are germane to the AHCY-like biological activity. It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Therefore considering the stat of art and the limited amount of guidance provided in the specification is unpredictable that the climed nucleotide sequences encodes an enzyme that has AHCY-like acitivity.

Response to arguments

The applicant argues that one of ordinary skill would have no difficulty in carrying out the invention as claimed based on the level of ordinary skill in this art taken with the

detailed description of the invention as presented in the originally filed application (response, page 6 para.2)

However, applicant's arguments are found NOT persuasive because applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). As stated in the earlier office action the office has clearly provided the evidence that the disclosed amino acid sequences of Seq ID NO:1 provided matches with a AHCY-type activity-like protein (Human SAHH), but with only 83% similarity. The state of art at the time of filing teaches that even though DD4b5.3 (SEQ ID NO:1) encodes an ACHY-like molecule the gene structure differs from that of AHCY (Dekker et al, Immunogenetics 53;993-1001, 2002., see page 998, col.2 para.2). Furthermore, the differences between AHCY and DCAL (encoded by SEQ ID NO:1) protein and gene structure strongly suggest that DCAL has a different substrate (page 1000, col.2 , para 4). Considering the state of art and lack of specific guidance in the instant specification it is unclear how one skill in the art would use the invention as claimed, since the specification fails to disclose a single functional assay for the enzyme activity encoded by the nucleotide sequences of SEQ ID NO:1 or any functional portion or equivalent thereof.

Since determining biological activity of a polypeptide base upon a low sequence similarity is not routine in the art, and without sufficient guidance to a specific functional assay experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed. The quantity of experimentation required would include the functional characterization of polypeptide encoded by SEQ ID NO: 1 as a protein having AHCY-like activity and use thereof.

3. Claims 4 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession of the claimed invention** for the same reasons of record as set forth in the office action mailed on 05/08/03.

The scope of invention as claimed encompasses a DNA sequence or a vector comprising the DNA sequence wherein the DNA encodes an enzyme or a functional portion or equivalent thereof.

Response to arguments

The applicant argues that one of ordinary skill would have no difficulty in carrying out the invention as claimed based on the level of ordinary skill in this art taken with the detailed description of the invention as presented in the originally filed application. The applicant further argues that it is clear that the applicant was in possession of the claimed invention at the time the application was filed (response, page 6 para.2).

However, applicant's argument are found NOT persuasive because the specification as filed fails to disclose any functional portion or equivalent of SEQ ID NO:1 which encodes an enzyme like ACHY. Applicant were referred to the Interim guidelines on ***Written Description*** published December 21, 1999 in the Federal Register, Vol. 64, No. 244, pp. 71427-71440. The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). At best the specification discloses the nucleotide sequence of SEQ ID NO:1. The specification fails to disclose any functional assay that is specific for the claimed enzyme activity explicitly or implicitly as putatively considered by the applicant. Even though DD4b5.3 (SEQ ID NO:1) encodes an ACHY-like molecule the gene structure differs from that of AHCY (Dekker et al, Immunogenetics 53;993-1001, 2002., see page 998, col.2 para.2). The differences between AHCY and DCAL (encoded by SEQ ID NO:1) protein and gene structure strongly suggest that DCAL has a different

substrate (page 1000, col.2, para 4). The general knowledge in the art concerning AHCY-like proteins encoded by the nucleotide sequence of SEQ ID NO:1 does not provide any indication as how the structure of one allele is representative of other unknown amino acid sequences having concordant or discordant functions. The commons attributes of all AHCY-like proteins are not described, and identifying attributes of variants other than SEQ ID NO:1 as claimed has not been described.

Furthermore, the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention *(Pfaff v. Wells Electronics, Inc 48 USPQ2d 1641, 1646 (1998)*. The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. *(see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000)*. In the instant case the nucleotide sequences encoding an ACHY-like polypeptide (as claimed) has been defined only by a statement of function of ACHY-like activity, which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claim Rejections - 35 USC § 102

4. Claims 18 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Hillier et al (Gen. Bank Acc. No. W00331, 04/15/96), for the same reasons of record as set forth in the office action mailed on 05/08/03.

The instant claim is drawn to a optionally labeled nucleic acid probe capable of hybridizing to the nucleic acid sequence of SEQ ID NO:1. The cited art teaches nucleic sequences which is 99% identical to nucleotide 1051-1435 of instant SE ID NO:1 (see

PTO sequence search report). Thus the cited art clearly anticipated a probe capable of hybridizing to SEQ ID NO:1.

Response to arguments

The applicant argues that Hillier does not anticipate the claimed subject matter. The applicant argues that the probe defined by claim 18 clearly encompasses other regions that are disclosed by the prior art. The applicant concluded that the subject matter of claim 18 is therefore novel over the Hillier disclosure.

However, applicant's argument are found NOT persuasive because Hillier clearly teaches a nucleotide sequence of 385 bp in length having 99% identity to the nucleotides sequences at position 1051-1435 of SEQ ID NO:1, which is capable of hybridizing to the nucleic acid sequences of SEQ ID NO:1. In addition the invention as claimed is not limited to any particular region of SEQ ID NO:1 or a probe identified by any specific nucleotide sequences. Thus the cited art clearly anticipate the invention as claimed.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sumesh Kaushal
Examiner Art Unit 1636

JEFFREY FREDMAN
PRIMARY EXAMINER